Selective cancer cell toxicity and radiosensitization using different high atomic number nanoparticles

Conference or Workshop Item

Selective cancer cell toxicity and radiosensitization using different high atomic number nanoparticles

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Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies

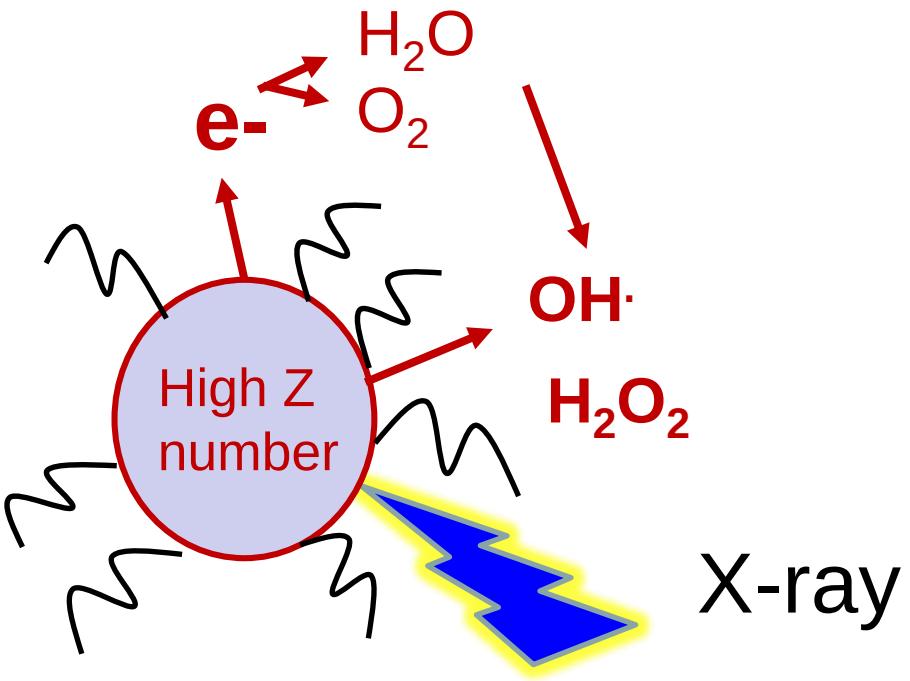
Radiotherapy = 50% of cancer treatments

EFFICIENT BUT:

- Toxic for surrounding tissues
- Radioresistance of several cancers
- Need to make radiotherapy selectively toxic for cancer cells

HOW ?

- Nanomaterials



Radiosensitization using nanoparticles (NPs)

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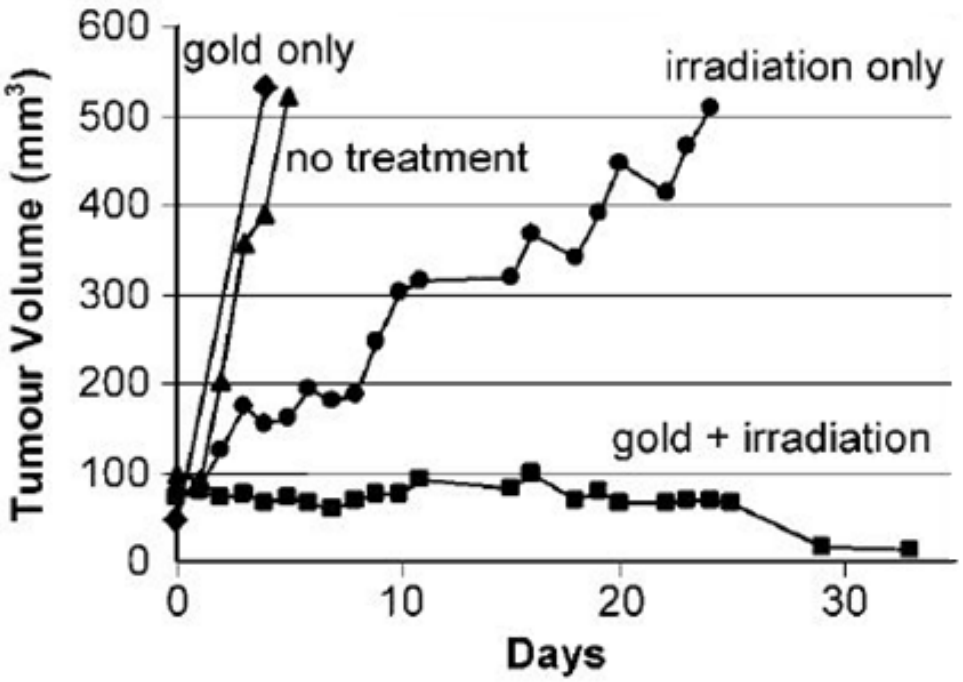
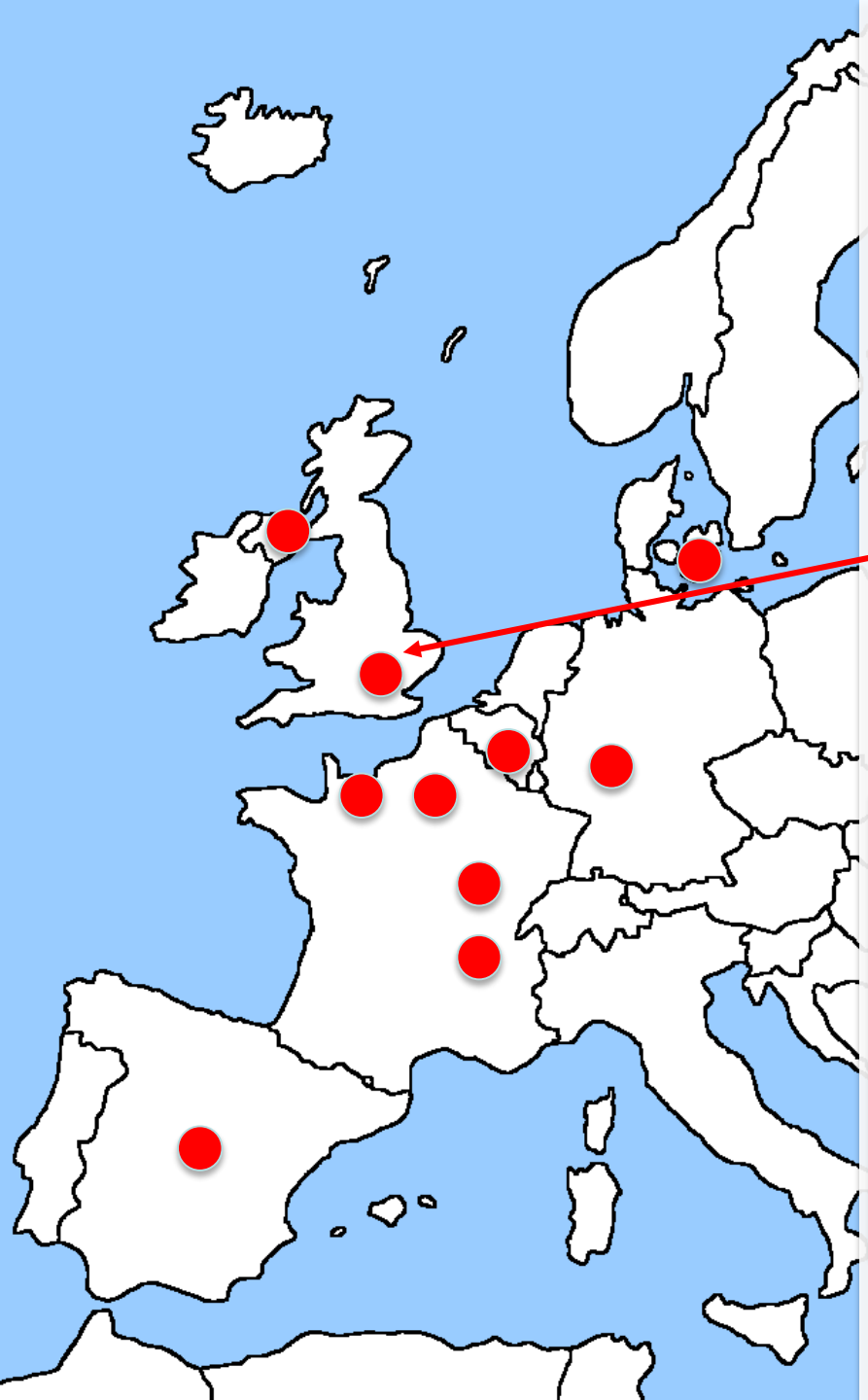
Previously shown for the first time with **kilovoltage** energies X-rays radiation

With Gold NPs
1.9 nm size



Average tumour volume on mice with or without treatment
Intravenous gold injection (1.35 g Au/kg)
Irradiation 30 Gy, 250 kVp, 2 min post injection
(Hainfeld *et al*, 2004, Physics in Medicine and Biology 49(18)

Further characterisation and optimisation needs to be done, especially using different types of energies



THE Argent PROJECT

Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies

Academic Partners

GSI Helmholtzzentrum für Schwerionenforschung GmbH

MBN Research Center

Queen's University Belfast

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The Open University

CSIC Consejo Superior de Investigaciones Científicas

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Industrial Partners

nano-H® Value-Added Nanotechnology

Quantum Wise

CheMatech macrocycle design technologies

Associated Partners

HIT Heidelberger Ionenstrahl-Therapiezentrum

Centre de Lutte contre le Cancer François Baclesse

Hospital Universitario Puerta de Hierro Majadahonda

SaludMadrid Comunidad de Madrid

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Minerva The knowledge brokers

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Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies

Irradiation
(Photons, X-rays, Protons and Heavy ions)

Synthesis of Nanoparticles

NANO → **MACRO**

Understanding Cellular Damage

Preclinical Evaluation

Theoretical Modelling & Experimentation

Main aims of research:

- Design, optimise and characterise nanoparticles for cancer radiotherapy

- Optimising radiosensitization by :

→ Selective targeting of cancer cells and organelles

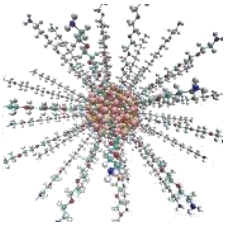
→ Increasing the level of oxidative stress

- Measure toxicity and potential effect on skin and breast *in vitro* model of two types of NPs:

→ Gold NPs (αGal/PEGamine coated)

→ Ceria NPs (cerium oxide)

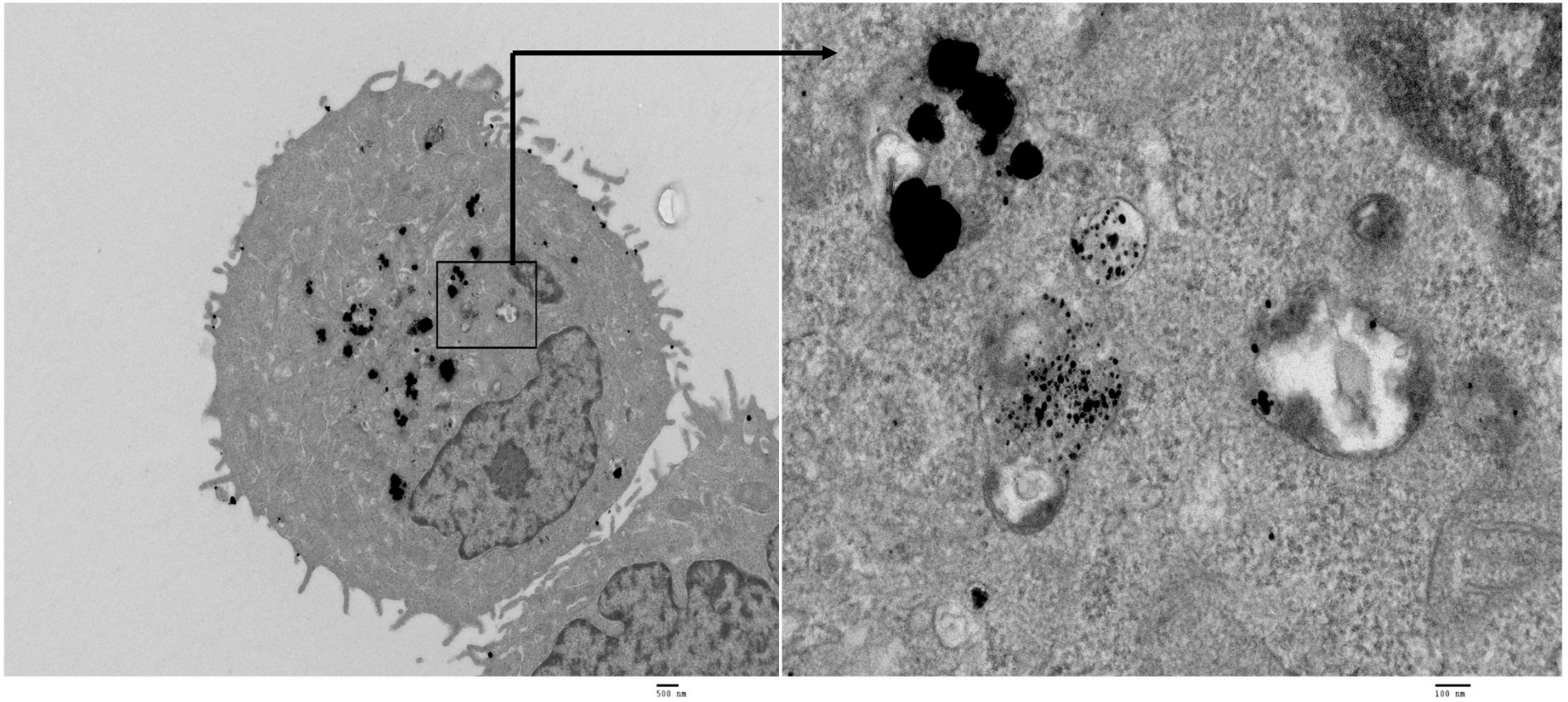
First results with skin models exposed to Gold NPs (AuNPs)



Z = 79

Average size 4.5 nm
αGal/PEGamine

Skin cancer cells ; 3 hrs of exposure, 10 µg/ml



AuNPs coated with αGal/PEGamine selectively accumulate in skin cancer cells, probably in lysosomes

First results with skin models exposed to Gold NPs (AuNPs)

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Skin normal cells; 3 hrs of exposure, 10 µg/ml

First results with skin models exposed to Gold NPs (AuNPs)

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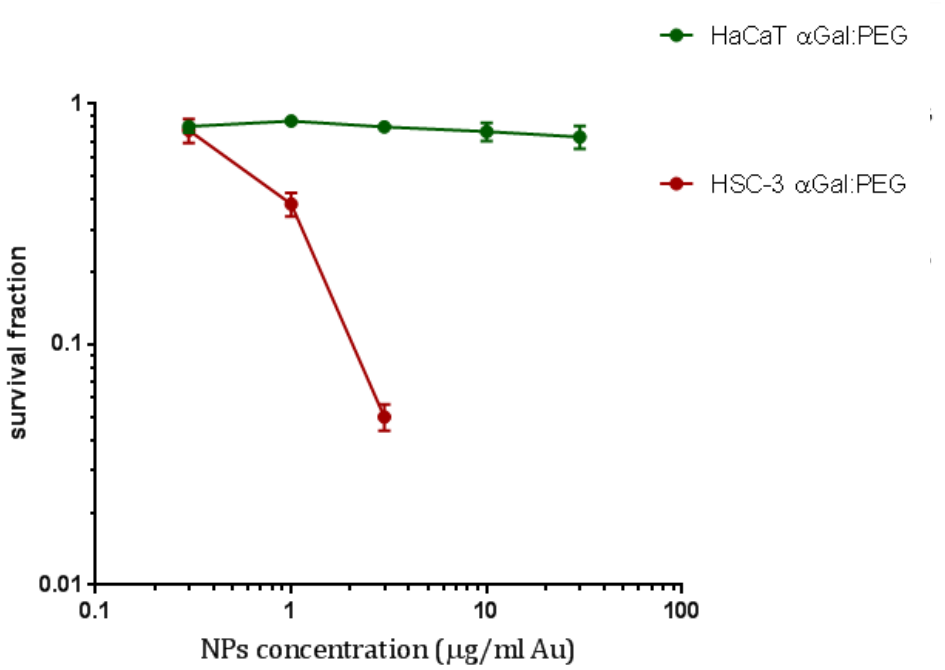
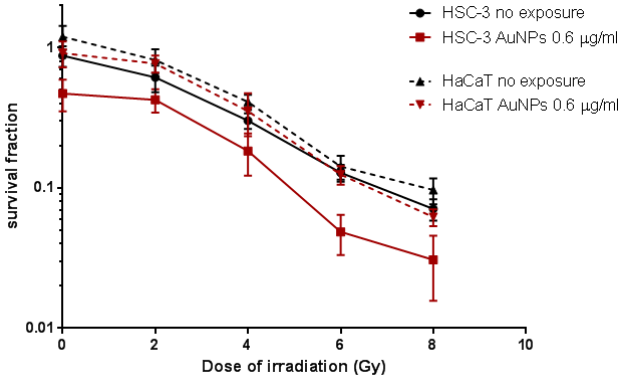
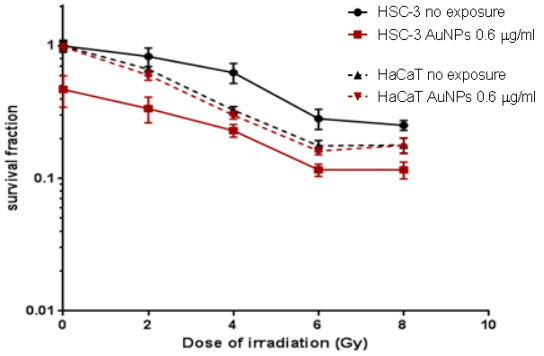
Dose vs response AuNPs 3h exposure



Cells exposed to 220 keV X-rays irradiation

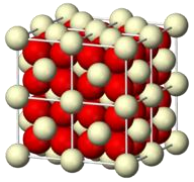


Cells exposed to 6 MeV X-rays irradiation



AuNPs coated with αGal/PEGamine are selectively toxic for skin cancer cells and give an additive effect in combination with X-ray radiotherapy

Cerium Oxide NPs (ceria NPs), characterization



Z = 58

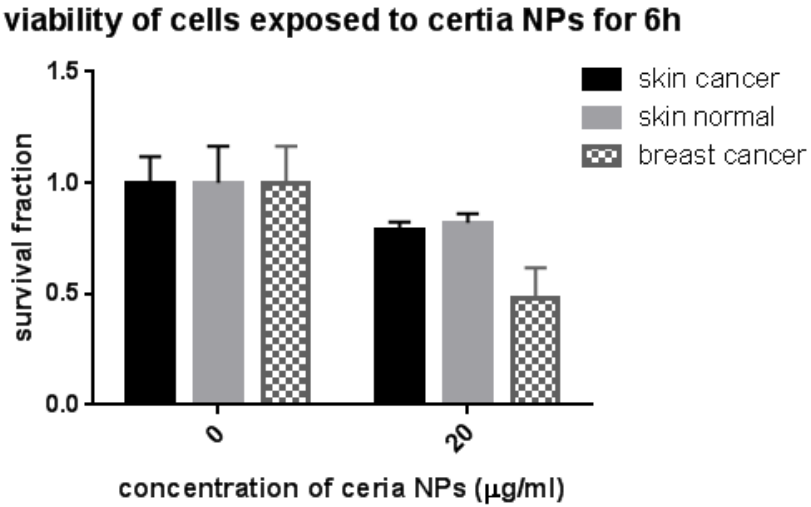
- Offer interesting properties as a large transport and storage of oxygen [1]
- Characterised as radioprotector or radiosensitiser depending on the pH[2] of the environment and the energy of irradiation [3]
- Few investigations on its potential as a radiosensitiser, nothing in combination with heavy elements

1. Goharshadi EK *et al.,(*2011). Journal of Colloid and Interface Science 356: 473-480
2. Gao Y *et al.*, (2014). OncoTargets and therapy 7: 835-840
3. Briggs A *et al.,(*2013). Nanomedicine: Nanotechnology, Biology and Medicine 9: 1098-1105

Cerium Oxide NPs, toxicity

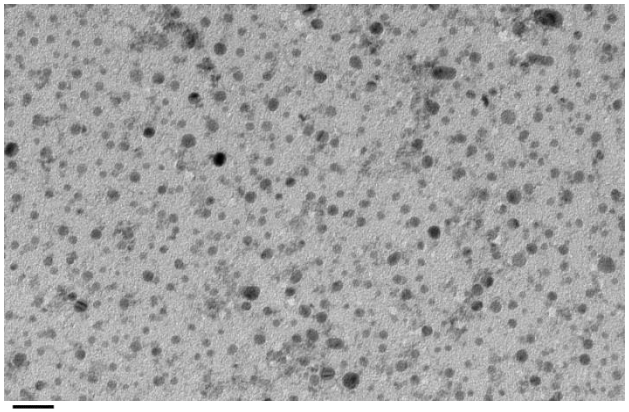
Explored on *in vitro* models, with a clonogenic assay

- Ceria NPs commercially available, average size of 5 nm



- Homemade (in collaboration with chemists at the Open University) in combination with bismuth or gold

Average size of 3 nm



20 nm TEM
HV=80.0kV Direct mag: 200000×

Summary and future work

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- **AuNPs** coated with αGal/PEGamine selectively toxic for skin cancer cells ; additive effect in combination with X-ray radiotherapy

- **Ceria NPs**, in combination with bismuth, gold

→ Could increase radiation induced oxidative stress in the tumour environment

<u>Any other types of NPs: high atomic number? Oxygen storage? Any ideas are welcome!</u>

These NPs will be tested on different cancer cells and in combination with radiotherapy.
A comparison between low energy and high energy photon will be explored

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